Remarks

Applicants have herein canceled claims 27, 50-53, 57, and 61, and amended claims 21, 28-44, 48-49, and 58-60, all without prejudice or disclaimer. Attached hereto is a marked-up version of the changes made by the current amendment, captioned "Version With Markings To Show Changes Made." In particular, claim 21 has been amended to recite the phrase "wherein said polypeptide promotes neuronal cell adhesion or axonal neurite extension." Claims 28-35 have been amended to cancel the subject matter of claim 34, and to rewrite claims 28-33 and 35 into independent form as requested by the Examiner. Claims 36-43 and 48-49 have been amended to recite the phrases "consisting of" and "consists of" instead of the phrases "comprising" and "comprises"; claim 36 has also been amended to recite the subject matter of previous claim 37, and claim 37 has also been amended to recite the phrase "at least 15 contiguous amino acids" instead of "at least 9 contiguous amino acids." Claim 44 has been amended to correct numbering and Markush format errors. Claims 58-60 have been amended to delete the terms "pharmaceutical" and "pharmaceutically acceptable". The amendments to the claims are fully supported by the specification as filed, and thus no new matter has been added.

Claims 21-26, 28-49, 54-56, and 58-60 are pending. Previous claims 28-33 and 35 have been indicated as allowable if rewritten in independent form. As pending claims 28-35 now contain the subject matter of previous claims 28-33 and 35 in independent form as requested by the Examiner, at the very least, pending claims 28-35 are now in form for allowance. Applicants respectfully request reconsideration of the remaining rejections in view of the following remarks.

I. Rejection of the Claims Under 35 U.S.C. § 112, First Paragraph

A. Written Description of Claims 38-42

The Examiner has rejected claims 38-42 under 35 U.S.C. § 112, first paragraph, alleging that:

> No proper antecedent nor conception in context of that described in the specification at the time of filing Applicants' invention is apparent for the broader concept of random epitope-bearing portions comprising "from about 75 to about 100/ about 168 to about 180/ about 204 to about 226/ about 258 to about 281/ about 291 to about 327 of SEQ ID NO:2" (i.e., as it relates to claims 38-42). In contrast to Applicants' assertions on page 7 of the first preliminary amendment, page 21 of the specification only

> contemplates specific "epitope-bearing portions" consisting of these amino acid position numbers; thereby constituting new matter.

Paper No. 14, pages 2-3, item 2 (emphasis added).

In response, Applicants respectfully disagree, and point out that the specification as filed fully supports claims 38-42. The specification at page 21, lines 24-29, provides explicit literal support for polypeptides comprising the range of epitope-bearing portions encompassed by claims 38-42:

> Non-limiting examples of antigenic polypeptides or peptides that can be used to generate NAF-1-specific antibodies include: a polypeptide comprising amino acid residues from about Pro-75 to about Gly-100; a polypeptide comprising amino acid residues from about Thr-168 to about Leu-180; a polypeptide comprising amino acid residues from about Asp-204 to about Ile-226; a polypeptide comprising amino acid residues from about Ile-258 to about Pro-281; and a polypeptide comprising amino acid residues from about Glu-291 to about Ser-327.

Specification, page 21, lines 24-29 (emphasis added).

Accordingly, the assertion that "the specification only contemplates specific 'epitope-bearing portions' consisting of these amino acid position numbers" (Paper No. 14, page 2-3; emphasis added) is an incorrect characterization of the specification's teachings. Hence, the previously pending claims were fully supported by an adequate written description sufficient to fulfill the requirements of 35 U.S.C. § 112, first paragraph.

However, Applicants note that claims 38-42 have been amended without prejudice or disclaimer to replace the "comprises" language with the phrase "wherein said portion consists of at least amino acids [X] to [Y]." Applicants reserve the right to pursue the originally claimed subject matter in one or more continuing applications. In light of the above, Applicants submit that the pending claims fully meet the written description requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the instant rejection be reconsidered and withdrawn.

B. Written Description of Claims 43-47

The Examiner has rejected claims 43-47 under 35 U.S.C. § 112, first paragraph, alleging that "no proper antecedent basis nor conception is apparent for the broader concept of 'comprising at least 10 contiguous amino acids of SEQ ID NO:2.'" Paper No. 14, page 3, first paragraph.

In response, Applicants respectfully disagree and traverse, as the specification provides a proper antecedent basis for these claims. More particularly, the specification teaches, *inter alia*, that:

> Thus, the present invention is directed to polynucleotides having at least a 70% identity, preferably at least 90% and more preferably at least a 95%, 96%, 97%, 98%, or 99% identity to a polynucleotide which encodes the polypeptide of SEQ ID NO:2 and polynucleotides complementary thereto as well as portions thereof, which portions have at least 30 consecutive bases and preferably at least 50 consecutive bases and to polypeptides encoded by such polynucleotides.
>
> Specification, at page 13, lines 5-10.

Therefore, since polynucleotides with at least 30 consecutive bases encode polypeptides of SEQ ID NO:2 with at least 10 contiguous amino acids, the specification *does* provide proper antecedent basis and conception for polypeptides consisting of at least 10 contiguous amino acids of SEQ ID NO:2. Indeed, to the extent that the Examiner is suggesting that the claim should instead recite "an isolated polypeptide encoded by a polynucleotide having at least 30 consecutive bases...," Applicants respectfully point out that "[t]he subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement." M.P.E.P. § 2163.02. Since one skilled in the art would clearly consider the subject matter to be the same, Applicants assert the written description requirement has been fully satisfied.

In light of the above, Applicants submit that the pending claims fully meet the written description requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the instant rejection be reconsidered and withdrawn.

C. Written Description of Claims 54-57 and 60

The Examiner has rejected claims 54-57 and 60 under 35 U.S.C. § 112, first paragraph, alleging that "[n]o proper antecedent nor conception in context of that described in the specification at the time of filing Applicants' invention is apparent for the broader concept of any polypeptide 'fused to' any 'heterologous polypeptide'." Paper No. 14, page 3, second paragraph. More particularly, the Examiner contends that the specification contemplates "only fusion with polypeptide sequences that 'aid in expression

and secretion of the polypeptide', or aid in purification of the polypeptides of the instant invention; thereby constituting new matter." *Id.*

In response, Applicants respectfully disagree and traverse. Preliminarily, as claim 57 has been canceled without prejudice or disclaimer, any rejection thereof has been obviated.

Applicants note that the Examiner is implicitly arguing that the specification does not sufficiently disclose the claimed genus of fusion proteins. However, "[t]he written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species." M.P.E.P. § 2163 at 2100-164. "What constitutes a 'representative number' is an inverse function of the skill and knowledge in the art." *Id.* Applicants note that the level of skill in the art of fusion proteins on the priority date of the present application was very high.

As noted above, the Examiner has accepted that the specification discloses several types of fusion proteins. In addition to the examples referred to by the Examiner, however, the specification also provides for fusion proteins made for numerous other purposes (in addition to aiding expression, secretion, or purification). For example, on page 13, lines 14-19, the specification teaches:

> To improve or alter the characteristics of NAF-1 polypeptides, protein engineering may be employed. Recombinant DNA technology known to those skilled in the art can be used to create novel mutant proteins or "muteins including single or multiple amino acid substitutions, deletions, additions or *fusion proteins*. Such modified polypeptides can show, *e.g.*, enhanced activity or increased stability. (emphasis added)

Accordingly, the specification describes many species of heterologous fusions comprising polypeptides of the present invention. Applicants respectfully assert that in light of the high level of skill in the art, the numerous species of heterologous fusion proteins described in the specification are a more than sufficient "representative number" to provide written description for the claimed genus of fusion proteins.

In light of the above, Applicants submit that the pending claims fully meet the written description requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the instant rejection be reconsidered and withdrawn.

D. Written Description of Claims 21-27, 34 & 36-61

The Examiner has rejected claims 21-27, 34 and 36-61 under 35 U.S.C. § 112, first paragraph. In particular, the Examiner asserted that:

> The specification describes the sole human polypeptide of SEQ ID NO:2. No other polypeptides are described from any other species... No adequate written description of what constitutes any different species, allelic variant (i.e., as both encompassed by the recitation of "at least 95%), or different open reading frame that merely "comprise" fragments of SEQ ID NO:2, or that "comprise" generic heterologous polypeptides fused to random fragments of SEQ ID NO:2 is provided within the instant specification, or known in the art...
>
> Paper No. 14, pages 3-4, item 3 (emphasis added).

In response, Applicants respectfully disagree.

With respect to claims 50-53, 57, and 61, Applicants maintain that the claims as previously pending were fully described in the specification such that one skilled in the art would reasonably conclude that the inventors had possession of the claimed invention. However, Applicants note that the subject matter of claims 50-53, 57, and 61 has been canceled without prejudice or disclaimer, thereby obviating any rejection of such claims. Applicants reserve the right to pursue the canceled subject matter in one or more continuing applications.

With respect to claims 21-27, 54, and 58, Applicants assert that the claims as previously pending were fully described in the specification, such that one skilled in the art would reasonably conclude that the inventors had possession of the claimed invention. However, Applicants note that the subject matter of previous claims 21(e) and 26 has been canceled without prejudice or disclaimer. Further, independent claim 21 (from which claims 22-25, 27, 54, and 58 depend) has been amended without prejudice or disclaimer to recite that the claimed polypeptide "promotes neuronal cell adhesion or axonal neurite extension." Applicants reserve the right to pursue the canceled subject matter in one or more continuing applications. Thus, as detailed in Example 14 of the Written Description Training Materials, claims 21-25, 27, 54, and 58 clearly meet the requirements of 35 U.S.C. § 112, first paragraph, as they do not embrace a "highly variant" genus.

With respect to claims 34, 36-49, 55-56, and 59-60, Applicants also maintain that the claims as previously pending were fully described in the specification, such that one skilled in the art would reasonably conclude that the inventors had possession of the

claimed invention. Indeed, it is well-established that a "gene is a chemical compound, albeit a complex one." *Amgen, Inc. v. Chugai Pharmaceutical Co., LTD.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). Thus, the claims of the instant application, directed to polypeptides consisting of at least a particular number of contiguous amino acid residues of SEQ ID NO:2 (or of the polypeptide encoded by the deposited clone), *i.e* , a genus of fragments of the NAF-1 polypeptide of the invention, are essentially chemical claims involving generic chemical formulas. As stated by Judge Lourie in *Eli Lilly*, "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass." All of the objectives met by a generic chemical formula are similarly met by the explicit description in the instant specification of both a polynucleotide and polypeptide sequence (i.e. SEQ ID NOS:1 & 2) and claims to polypeptides consisting of at least, *inter alia*, 10 contiguous amino acid residues of that sequence. That is, the instant claims clearly distinguish the boundaries of each claimed genus and identify all of the members of each genus. Accordingly, one skilled in the art would reasonably conclude that Applicants had possession of the polypeptides encompassed by the rejected claims, upon reading the present application as filed.

In particular, the skilled artisan could clearly envision and identify by specific amino acid sequence the individual polypeptides containing fragments of at least, *inter alia*, 10 contiguous amino acids of SEQ ID NO:2 of the invention, including the following members of the claimed genus:

- each of the 10mer polypeptides of SEQ ID NO:2 as a progression from -23 to -14, -22 to -13, etc.;
- for any given 10mer of SEQ ID NO:2, such as the 10mer from amino acids 1 to 10, each of the polypeptides that adds, sequentially, an additional amino acid in the C-terminal direction of SEQ ID NO:2 (e.g., 1 to 11, 1 to 12, etc.); and, similarly, each polypeptide that adds an additional amino acid sequentially in the N-terminal direction (e.g., -1 to 10, -2 to 10, etc.); or a combination thereof; and
- each of the polypeptides produced by a deletion from the N-terminal methionine of SEQ ID NO:2 up through position 298 (e.g., -22 to 308, -21 to

308, etc., up to 299 to 308); as well as each of the polypeptides produced by a deletion from the C-terminal residue through up through position -13 (e.g., -23 to 307, -23 to 306, etc., up to -23 to -14).

Nothing more than what is described in the specification would be required to identify every single one of the polypeptides containing, *e.g.*, at least 10 contiguous amino acids of the NAF-1 protein. Clearly, such knowledge is well within what is expected of the skilled artisan. Further, the instant claims do not require the claimed polypeptides to possess any particular activity or characteristic beyond the described sequence, and the subject matter of what is claimed is fully supported by the specification. § 112 requires no more. *See Union Oil Co. v. Atlantic Richfield Co.*, 208 F.3d 989, 1000, 54 U.S.P.Q.2d 1227 (Fed. Cir. 2000); M.P.E.P. § 2163.02.

However, Applicants note that the subject matter of previous claim 34 has been canceled without prejudice or disclaimer (present claim 34 contains the subject matter of previous claim 35, as noted above). Further, claims 36-43 and 48-49 (from which claims 44-47, 54-56, and 59-60 depend) have been amended without prejudice or disclaimer to recite the phrases "consisting of" and "consists of", rather than the phrases "comprising" and "comprises". Applicants reserve the right to pursue the originally claimed subject matter in one or more continuing applications. In light of the above, Applicants submit that the pending claims fully meet the written description requirements of 35 U.S.C. § 112, first paragraph.

For all of the above reasons, Applicants respectfully assert that the specification conveys with reasonable clarity that Applicants were in possession of the claimed invention. Therefore, Applicants submit that the pending claims fully meet the written description requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the instant rejection of the claims be reconsidered and withdrawn.

E. Enablement of Claims 21-27, 34 and 36-61

The Examiner has also rejected claims 21-27, 34 and 36-61 under 35 U.S.C. § 112, first paragraph, alleging that "the specification, while being enabling for the specific polypeptide depicted as SEQ ID NO:2, does not reasonably provide enablement for any biological functional equivalent polypeptides/fragments with little structural

characterization and no distinguishable recited functional characteristics." Paper No. 14, page 4, item 4. More particularly, the Examiner contends that:

> [T]he specification does not teach which particular amino acids are critical for any NAF-1 protein's function, nor how to distinguish such from any different polypeptide sequence that possesses none of the desired functions of the instant invention. Moreover, random mutations and/or random truncated variants of different NAF-1 related polypeptides would be expected by the skilled artisan to result in generation of inactive proteins.

Paper No. 14, page 5, first paragraph, sentences 3-4.

Applicants respectfully disagree and traverse. As an initial matter, Applicants note that as discussed above, the subject matter of previous claims 21(e), 26, 34, 50-53, 57, and 61 has been canceled without prejudice or disclaimer, thereby obviating any rejection of those claims. Further, independent claim 21 (from which claims 22-25, 27, 54, and 58 depend) has been amended without prejudice or disclaimer to recite that the claimed polypeptide "promotes neuronal cell adhesion or axonal neurite extension." Claims 36-43 and 48-49 (from which claims 44-47, 54-56, and 59-60 depend) have also been amended without prejudice or disclaimer to recite the phrases "consisting of" and "consists of", rather than the phrases "comprising" and "comprises".

With respect to the pending claims, M.P.E.P. § 2164.01(b) states that "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement is satisfied." *See also In re Fisher*, 427 F.2d 833, 839 166 U.S.P.Q. 18, 24 (CCPA 1970). The Federal Circuit has also held that making the claimed species and screening them for the desired function is acceptable, so long as the experimentation is not undue. *See In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988).

In the present case, the specification provides methods which may be used by those of ordinary skill in the art to make and test NAF-1 polypeptide variants without undue experimentation. In particular, the specification teaches *in vitro* assays that may be used to distinguish polypeptides with NAF-1 activity from those that may not have such activity. For example, the specification at page 10, lines 19-33, teaches that polypeptides of the invention can be assayed for ability to cause axonal neurite extension or promote neural

cell adhesion as described in Klar *et al.*, *Cell* 69:95-110 (incorporated by reference in the present specification).

Further, the specification provides extensive guidance to enable the skilled artisan as to the regions of the disclosed polypeptide that are responsible for the interactions underlying its biological functions. In addition to disclosing the nucleotide and amino acid sequences, the specification provides a detailed analysis of the structural and functional attributes of NAF-1, including, *e.g.*, an amino acid alignment of NAF-1 with a similar rat protein (Figure 2); comparison of consensus functional motifs within NAF-1 (cell-adhesion sequence) compared to rat F-spondin (Figure 3); and a profile of the predicted alpha, beta, turn, coil, hydrophobic, hydrophilic, amphipathic, flexible, surface and antigenic regions (*i.e.*, epitope-bearing portions) of NAF-1 (Figure 4). *See also* page 4. Knowledge of such regions of a polypeptide can serve as a guide to the skilled artisan, identifying those regions that tolerate only relative conservative substitutions or no substitutions. Thus, one of skill in the art would be able to predict with reasonable certainty which variants would have activity or antigenicity. Thus, by disclosing, *inter alia*, the antigenic regions of NAF-1, Applicants have identified regions of the polypeptide that can tolerate only relative conservative substitutions or no substitutions, which, conversely, enables one of skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change.

While the Examiner contends that "random mutations and/or random truncated variants of different NAF-1 related polypeptides would be expected by the skilled artisan to result in generation of inactive proteins," (Paper No. 14 at page 5), Applicants assert that most such substitutions or truncations will not disrupt the biological activity or immunogenicity of the NAF-1 protein. *See, e.g.*, page 13, line 21 to page 16, line 16 (citing Ron *et al.*, Dobeli *et al.*, and Bowie *et al.*). Moreover, as discussed above, the specification provides extensive guidance to the skilled artisan, so that such mutations and truncations would not merely be "random." Even assuming *arguendo* that some of the claimed polypeptides would lack either the biological activity or immunogenicity of the full length NAF-1 polypeptide, Applicants point out that "it is not a function of the claims to specifically exclude ... possible inoperative substances." *Atlas Powder Co. v. E.I. DuPont de Nemours*, 750 F.2d 1569, 1576, 224 U.S.P.Q. 409 (Fed. Cir. 1984). *See also In re Wands*, 858 F.2d at 737-38.

Further, the only evidence provided by the Examiner in support of the rejection and the assertion that "the significance of particular amino acid sequences for different aspects of biological activity cannot be predicted a priori but must be determined from case to case by painstaking experimental study," (Paper No. 14, page 5), is a publication by Rudinger. Applicants respectfully disagree with the assertion, and point out that Rudinger was published in June of 1976, four months short of twenty years before the priority date of the present application. However, it is the state of the art "at the filing date of the application" that must be used to determine whether a particular disclosure is enabling. M.P.E.P. § 2164.05(a). Indeed, the M.P.E.P. specifically cautions against the use of dated references such as Rudinger:

> The state of the art for a given technology is not static in time. It is entirely possible that a disclosure filed on January 2, 1990, would not have been enabled. However, if the same disclosure had been filed on January 2, 1996, it might have enabled the claims. Therefore, the state of the prior art must be evaluated for each application based on its filing date.

Applicants agree that some aspects of the present application would have either required "painstaking experimental study" or would have been completely impossible in 1976, when the entire field of molecular biology was in its infancy. However, while the methods and techniques relied upon in the present application may have required "painstaking experimental study" in 1976, these methods and techniques were routinely use by those of ordinary skill in the art by 1996, as evidenced in part by the many publications referenced in the specification. Thus, as Rudinger only reflects the state of the art nearly twenty years before the critical date, it cannot serve to support an enablement rejection for an application filed in 1996.

In view of the above, Applicants assert that the specification enables one skilled in the art to make and use the claimed polypeptides without undue experimentation. Thus, Applicants respectfully request that the Examiner's rejection of claims 21-27, 34 and 36-61 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

II. Rejection of the Claims Under 35 U.S.C. § 112, Second Paragraph

A. "Complement"

Claims 50-53, 57 and 61 were rejected under 35 U.S.C. § 112, second paragraph. In particular, the Examiner pointed out that only the sense strand can encode the NAF-1

polypeptide, whereas claim 50 (and thereby dependent claims 51-53, 57 and 61) implies that both sense and anti-sense strands encode the NAF-1 polypeptide.

However, as noted above, claims 50-53, 57 and 61 have been canceled without prejudice or disclaimer, thereby obviating the instant rejection. Accordingly, Applicants respectfully request that the rejection of claims 50-53, 57 and 61 under 35 U.S.C. § 112, second paragraph be reconsidered and withdrawn.

B. "Pharmaceutical"

Claims 58-61 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being "indefinite." In particular, it was asserted that:

> It is ambiguous how polypeptides merely comprising "epitope-bearing portions", or that merely "bind to an antibody specific to a polypeptide" can be used in a pharmaceutical composition, or how a polypeptide merely comprising "at least 10 contiguous amino acids" or merely comprising other fragments of SEQ ID NO:2 with no recited functional requirements related to a pharmaceutical use are to be used in a pharmaceutical composition.

Paper No. 14, pages 6-7, item 6 (emphasis added).

In response, Applicants respectfully disagree, and assert that the present specification provides (in addition to that which was known by those of ordinary skill) written description of how the polypeptides may be used in a pharmaceutical composition. *See, e.g.*, Specification at pages 29, lines 31-37, and page 30, lines 1-36. Nevertheless, as noted above, claim 61 has been canceled without prejudice or disclaimer, and claims 58-60 have been amended without prejudice or disclaimer to remove the terms "pharmaceutical" and "pharmaceutically acceptable". Accordingly, the rejection of claims 58-61 under 35 U.S.C. § 112, second paragraph, should be reconsidered and withdrawn.

III. Rejection of the Claims Under 35 U.S.C. § 102

Claims 36 and 55 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Jessell et al. (U.S. Patent 5,279,966). *See* Paper No. 14, page 7, item 7. In particular, it was asserted that "Jessell et al teach rat F-spondin ...comprises at least 7 contiguous amino acids of SEQ ID NO:2..." *Id.*

In response, as noted above, Applicants have amended claim 36 (from which claim 55 depends) without prejudice or disclaimer to recite "at least 9 contiguous amino acids" rather than "at least 7 contiguous amino acids." Applicants note that the rat F-spondin protein of Jessell, et al. does not disclose nine contiguous amino acids of SEQ ID NO:2. Support for amended claim 36 can be found in the specification as filed at, for example, page 21, lines 19-22. Thus, no new matter has been added.

Claims 50-53, 57, and 61 were also rejected, based on the assertion that:

> Jessell's polypeptide is encoded by a polynucleotide that would inherently hybridize under stringent conditions to residue #580-599 of SEQ ID NO:1, and because Jessell's polypeptide possesses axonal neurite extension/outgrowth, neural adhesion and antibody binding activity...and because Jessell et al. disclose pharmaceutical compositions of their protein, the limitations of claims 50-53, 57, 59 & 61 are also met.

Paper No. 14, page 7, item 7.

In response, as noted above, claims 50-53, 57, and 61 have been canceled without prejudice or disclaimer, thereby obviating the instant rejection.

In view of the above, Applicants assert that the rejections set forth by the Examiner have been obviated, and thus respectfully request that the rejection of claims 36, 50-53, 55, 57, and 61 under 35 U.S.C. § 102(b) be reconsidered and withdrawn.

Conclusion

Applicants believe that this application is in condition for allowance, and an early notice to that effect is urged. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicants would expedite the allowance of this application.

Applicants believe that there are no fees due in connection with the filing of this paper. However, should a fee be due, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an

extension is requested and the appropriate fee should also be charged to our Deposit Account.

Respectfully submitted,

Dated: January 3, 2003

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KKH/MJH/DAS
Enclosures

CERTIFICATE OF TRANSMISSION UNDER 37 C.F.R. § 1.8

1. Fax Cover
2. Amendment And Reply Under 37 C.F.R. 1.111
3. Version With Markings To Show Changes Made
4. Certificate of Transmission Under 37 C.F.R. § 1.8

I hereby certify that the above-listed correspondence is being facsimile transmitted to the United States Patent and Trademark Office on January 3, 2003.

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VIA FACSIMILE JANUARY 3, 2003

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Hastings, et al.

Docket No.: PF226D1

Application No.: 09/170,042

Group Art Unit: 1647

Filed: October 13, 1998

Examiner: R.C. Hayes

For: Human Neuronal Attachment Factor-1

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claims 27, 50-53, 57, and 61 have been canceled without prejudice or disclaimer. Claims 21, 28-44, 48-49, and 58-60 have been rewritten as follows:

21. (Once amended) An isolated polypeptide comprising an amino acid sequence which is at least 95% identical to a member selected from the group consisting of:

(a) amino acids 1 to 331 of SEQ ID NO:2 or the complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97343;

(b) amino acids 2 to 331 of SEQ ID NO:2 or the complete amino acid sequence excepting the N-terminal methionine encoded by the cDNA clone contained in ATCC Deposit No. 97343;

(c) amino acids 24 to 331 of SEQ ID NO:2;

(d) amino acids 27 to 331 of SEQ ID NO:2; and

(e) ~~amino acids 284 to 330 of SEQ ID NO:2; and~~

~~(f)~~ the amino acid sequence of the mature form of Neuronal Attachment Factor-1 (NAF-1) encoded by the cDNA clone contained in ATCC Deposit No. 97343;

wherein said polypeptide promotes neuronal cell adhesion or axonal neurite extension ~~percentage of identity is determined using the Bestfit program with parameters set such that the percentage of identity is calculated over the full length of the reference sequence and gaps of up to 5% of the total number of residues in the reference sequence~~

~~are allowed, and wherein up to 5% of the amino acid residues in the reference sequence may be deleted or substituted with another amino acid, or a number of amino acids up to 5% of the total amino acid residues in the reference sequence may be inserted into the reference sequence~~.

28. (Once amended) ~~The~~ An isolated polypeptide comprising an amino acid sequence selected from the group consisting of: ~~of claim 21, wherein said polypeptide comprises~~

(a) ~~the amino acid sequence of~~ amino acids 1 to 331 of SEQ ID NO:2~~.~~;

(b) the complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97343;

(c) amino acids 2 to 331 of SEQ ID NO:2;

(d) the complete amino acid sequence excepting the N-terminal methionine encoded by the cDNA clone contained in ATCC Deposit No. 97343;

(e) amino acids 24 to 331 of SEQ ID NO:2;

(f) amino acids 27 to 331 of SEQ ID NO:2; and

(g) the amino acid sequence of the mature form of NAF-1 encoded by the cDNA clone contained in ATCC Deposit No. 97343.

29. (Once amended) The isolated polypeptide of claim ~~21~~ 28 wherein said ~~polypeptide comprises the complete~~ amino acid sequence is (a) ~~encoded by the cDNA clone contained in ATCC Deposit No. 97343~~.

30. (Once amended) The isolated polypeptide of claim ~~21~~ 28 wherein said ~~polypeptide comprises the~~ amino acid sequence is (b) ~~of amino acids 2 to 331 of SEQ ID NO:2~~.

31. (Once amended) The isolated polypeptide of claim ~~21~~ 28 wherein said ~~polypeptide comprises the complete~~ amino acid sequence is (c) ~~excepting the N-terminal methionine encoded by the cDNA clone contained in ATCC Deposit No. 97343~~.

32. (Once amended) The isolated polypeptide of claim ~~21~~ 28 wherein said ~~polypeptide comprises the~~ amino acid sequence is (d) ~~of amino acids 24 to 331 of SEQ ID NO:2~~.

33. (Once amended) The isolated polypeptide of claim ~~21~~ 28 wherein said ~~polypeptide comprises the~~ amino acid sequence is (e) ~~of amino acids 27 to 331 of SEQ ID NO:2~~.

34. (Once amended) The isolated polypeptide of claim ~~21~~ 28 wherein said ~~polypeptide comprises the~~ amino acid sequence is (f) ~~of amino acids 284 to 330 of SEQ ID NO:2~~.

35. (Once amended) The isolated polypeptide of claim ~~21~~ 28~~,~~ wherein said ~~polypeptide comprises the~~ amino acid sequence is (g) ~~of the mature form of NAF-1 encoded by the cDNA clone contained in ATCC Deposit No. 97343~~.

36. (Once amended) An epitope-bearing portion of the NAF-1 polypeptide ~~comprising~~ consisting of at least ~~7~~ 9 contiguous amino acids of SEQ ID NO:2.

37. (Once amended) The epitope-bearing portion of claim 36, which ~~comprises~~ consists of at least ~~9~~ 15 contiguous amino acids of SEQ ID NO:2.

38. (Once amended) The epitope-bearing portion of claim 36, ~~which comprises~~ wherein said portion consists of at least amino acids ~~from about~~ 75 to ~~about~~ 100 of SEQ ID NO:2.

39. (Once amended) The epitope-bearing portion of claim 36, ~~which comprises~~ wherein said portion consists of at least amino acids ~~from about~~ 168 to ~~about~~ 180 of SEQ ID NO:2.

40. (Once amended) The epitope-bearing portion of claim 36, ~~which comprises~~ wherein said portion consists of at least amino acids ~~from about~~ 204 to ~~about~~ 226 of SEQ ID NO:2.

41. (Once amended) The epitope-bearing portion of claim 36, ~~which comprises~~ wherein said portion consists of at least amino acids ~~from about~~ 258 to ~~about~~ 281 of SEQ ID NO:2.

42. (Once amended) The epitope-bearing portion of claim 36, ~~which comprises~~ wherein said portion consists of at least amino acids ~~from about~~ 291 to ~~about~~ 327 of SEQ ID NO:2.

43. (Once amended) An isolated polypeptide ~~comprising~~ consisting of at least 10 contiguous amino acids of SEQ ID NO:2.

44. (Once amended) The isolated polypeptide of claim 43, which has at least one activity selected from the group consisting of:

(a) promotes axonal neurite extension;

(b) promotes neural cell adhesion; or

~~(b)~~(c) binds to an antibody specific to the polypeptide of SEQ ID NO:2.

48. (Once amended) The isolated polypeptide of claim 43, which ~~comprises~~ consists of at least 30 contiguous amino acids of SEQ ID NO:2.

49. (Once amended) The isolated polypeptide of claim 43, which ~~comprises~~ consists of at least 50 contiguous amino acids of SEQ ID NO:2.

58. (Once amended) A ~~pharmaceutical~~ composition comprising the polypeptide of claim 21 and a ~~pharmaceutically acceptable~~ carrier.

59. (Once amended) A ~~pharmaceutical~~ composition comprising the polypeptide of claim 36 and a ~~pharmaceutically acceptable~~ carrier.

60. (Once amended) A ~~pharmaceutical~~ composition comprising the polypeptide of claim 43 and a ~~pharmaceutically acceptable~~ carrier.